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Docket No: C38435/109700CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
Akira ASAKURA *et al.*	)	Examiner: M. Walicka
Serial No.: 09/470,667	)	Art Unit: 1652
Filed: December 22, 1999	)	
For: **NOVEL ALCOHOL/ALDEHYDE DEHYDROGENASES**	)	

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF MR. YOSHITAKA MURATA UNDER 37 C.F.R. § 1.132

Sir:

I, Yoshitaka Murata, a citizen and resident of Japan, hereby declare as follows:

1. I am employed by K.K. Kyurin Corporation, 27-25, Morishita-cho, Yahatanishi-ku, Kitakyushu-shi, Fukuoka-ken, 806-0046 Japan ("Kyurin"). I hold the position of Scientist (Kyurin Omtest Laboratory Dept. "KOLA") at Kyurin. One of my duties at Kyurin is to coordinate the preparation of chromosomal DNA from various cell lines in response to orders from clients of Kyurin. A copy of my *curriculum vitae* is attached as Exhibit 1.

2. By way of background, Kyurin is an independent commercial entity that is not affiliated with the Nippon Roche Research Center of

Nippon Roche K.K. ("NRKK"). Among the services provided by Kyurin to its clients is the preparation of chromosomal DNA from various kinds of cell lines. It is in this capacity that I was contacted by Mr. Masao Mashita of Sawady Technology Co., Ltd., 1-29-10, Maeno-cho, Itabashi-ku, Tokyo, Japan 174-0063 ("Sawady") regarding our ability and interest in preparing chromosomal DNA by reconstituting and growing up a lyophilized sample of *Gluconobacter oxydans* DSM 4025 as set forth in more detail below.

3. At the beginning of August, 2000, I was asked by Mr. Mashita to have Kyurin reconstitute, grow up, and harvest chromosomal DNA from a lyophilized sample of *Gluconobacter oxydans* DSM 4025 cells that he would provide to me.

4. On August 10, Mr. Mashita sent a letter to Kyurin via facsimile (a copy of the original facsimile in Japanese is attached as Exhibit 2 and its translation in English is attached as Exhibit 3). This letter confirmed our agreement with Sawady that Kyurin would conduct the requested work and included an "ORDER FORM" (original written in Japanese, a copy of which is attached as Exhibit 4; its English translation is attached as Exhibit 5) and a set of "GENERAL PROTOCOLS" (original written in English, Exhibit 6; its Japanese translation as Exhibit 7) describing the methods to be used by us for isolating the requested chromosomal DNA.

5. On August 18, 2000, I received a package from Mr. Mashita via overnight courier. The package contained an ampoule identified as containing lyophilized cells of *Gluconobacter oxydans* DSM 4025 and an order sheet from Sawady (original written in Japanese, a copy of which is attached as Exhibit 8; its English translation is attached as Exhibit 9).

6. As soon as I received the package, I stored the package in a refrigerator accessible only to authorized Kyurin personnel at 4°C. Later that day, Dr. Sugama, Director, KOLA Kyurin, at my direction, sent an e-mail to Mr. Mashita to confirm receipt of the ampoule and the order letter.

7. On August 26, 2000, I gave Ms. Masako Nomaguchi, a researcher employed by Kyurin, the ampoule I received from Mr. Mashita on August 18, 2000, identified as containing lyophilized cells of *Gluconobacter oxydans* DSM 4025, and instructed Ms. Nomaguchi to reconstitute the lyophilized cells contained in the ampoule, to grow up those cells, and to isolate chromosomal DNA from those cells.

8. On August 31, 2000, Ms. Nomaguchi informed me that she had completed isolating the chromosomal DNA from the cells grown up from the *Gluconobacter oxydans* DSM 4025 sample I had given her, which I had received from Mr. Mashita on August 18, 2000. Ms.

Nomaguchi collected the isolated chromosomal DNA in a 1.5ml tube, which was labeled "SW-2 / DNeasy 28ng / μl 000831 * SW-2 / Sepagene 0.508 μg / μl 000831."

9. On August 31, 2000, I placed the 1.5ml tube labeled "SW-2 / DNeasy 28ng / μl 000831 * SW-2 / Sepagene 0.508 μg / μl 000831" containing the isolated chromosomal DNA prepared by Ms. Nomaguchi into a shipping package. That same day, I forwarded to Mr. Mashita the package containing the tube labeled "SW-2 / DNeasy 28ng / μl 000831 * SW-2 / Sepagene 0.508 μg / μl 000831" containing the chromosomal DNA isolated from the *Gluconobacter oxydans* DSM 4025 cells prepared by Ms. Nomaguchi.

10. In sum, the ampoule containing the lyophilized *Gluconobacter oxydans* DSM 4025 cells that I received from Mr. Mashita on August 18, 2000 was the same ampoule that I gave to Ms. Nomaguchi, who reconstituted the cells, grew them up, and isolated genomic DNA from them. And, the chromosomal DNA that Ms. Nomaguchi isolated from the reconstituted *Gluconobacter oxydans* DSM 4025 cells was the same DNA contained in the tube labeled "SW-2 / DNeasy 28ng / μl 000831 * SW-2 / Sepagene 0.508 μg / μl 000831" that I forwarded to Mr. Mashita on August 31, 2000.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: September 11, 2002

Yoshitaka Murata

Yoshitaka Murata

CURRICULUM VITAE of Yoshitaka Murata

Scientist
K.K. Kyurin Corporation,
Address 27-25, Morishita-cho, Yahatanishi-ku, Kitakyushu-shi, Fukuoka-ken, 806-0046 Japan

Phone: +81-93-642-3911
FAX: +81-93-642-3967
E-mail: kola@kyurin.co.jp

Education & Research Experience:

1. Present Title
Scientist at K. K. Kyurin Corporation

2. Master Degree (April 1994 to March 1996)
Master in Chemistry from Department of Chemistry, Faculty of Science, Fukuoka University, Japan.
The title of Master thesis:
"Involvement of Cytoskeletal Proteins in the Membrane Stability of Human Erythrocytes under Hydrostatic Pressure" instructed by Prof. Shigeyuki Terada

3. Bachelor Degree (April 1990 to March 1994)
Department of Chemistry, Faculty of Science, Fukuoka University, Japan.
The title of Bachelor thesis:
"Effect of distribution of phospholipids in the Membrane on the Hemolysis of Human Erythrocytes under Hydrostatic Pressure" instructed by Prof. Eiji Kimoto

4. Professional field
Molecular biology, Genetic engineering

5. Memberships

a) Japanese Society for Immunology

6. Personal information:

Male

Japanese citizen,

Birthday: July 7, 1970

LIST OF PUBLICATIONS

Original Papers

Yamaguchi T, Murata Y, Kobayashi J, Kimoto E. (1994) Effects of chemical modification of membrane thiol groups on hemolysis of human erythrocytes under hydrostatic pressure. **Biochim Biophys Acta 1195: 205-10**

----------END of CV----------

received
Aug. 17, 2002
M. Shingo

FAX送信表

平成12年 8月10日

送信先

KYURIN
MEDICAL LABORATORY

KOLA
(KYURIN Omtest Laboratory Dept.)
研究員 野間口 雅子

株式会社キューリン
北九州市八幡西区森下町27番25号 〒806-0046
TEL093-642-3911㈹ FAX093-642-3967

発信元

〒171 東京都豊島区南池袋2－9－9 第1池袋ホワイトビル1F
(株)サワディーテクノロジー
PHONE 03-3988-4633 FAX 03-3982-5666

用 件／新規オーダー

前略

先日 洲鎌さんへ連絡した件ですが、正式に発注になりました。菌体からプロモゾンDNA抽出1、リアルPCR 2点をお願いします。概算で結構ですので、御見積をお願いします。

草々

送信枚数 本表含め 2枚

担当者 簡下

Declaration Y. Murata
Exhibit-2

17/26

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[T4] FAX from Mr. Mashita to Kyurin, KOLA dated Aug. 10, 2000

To: KYURIN, KOLA (KYURIN Omtest Laboratory Dept.)
Researcher Masako Nomaguchi
K.K. Kyurin Corporation, 27-25, Morishita-cho, Yahatanishi-ku,
Kitakyushu-shi, Fukuoka-ken, 806-0046
TEL 093-642-3911(Representative) FAX 093-642-3967

From: K.K. Sawady Technology
Dai-ichi Ikebukuro White Building 1F
2-9-9, Minami-Ikebukuro, Toshima-ku, Tokyo, 171
PHONE 03-3988-4633 FAX 03-3982-5666

Date: August 10, 2000

Subject: New order

Hello,

The subject I informed Mr. Sugama was officially ordered. Please extract chromosomal DNA from cells and do RT-PCR*. Please let me know approximate estimate.

Best regards,

Masako Mashita

Declaration K. Murata
Exhibit 4-3

19/26

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株式会社サワデーテクノロジー御中
遺伝子塩基配列解析依頼書
(発注)

---

1. 依頼日: ２０００年８月　日

Declaration K. Murata
Exhibit-4 (1/2)

2. 依頼者

氏名: 星野達雄
所属: 応用微生物部
日本ロシュ研究所 日本ロシュ株式会社
所在地: 〒247-8530 神奈川県鎌倉市梶原 200
TEL : 0467-47-2226 (Ext. 3116) FAX : 0467-45-6812
(お問い合わせ先：新城雅子, Ph.D／e-mail : masako.shinjoh@roche.com)

3. 解析結果送付先： 依頼者直送

4. サンプル解析方法

PCR 生成物の直接配列決定 [添付の GENERAL PROTOCOLS をご参照下さい]

5. オプション: [８.その他の項をご参照下さい]

6. 解析サンプル記述欄

解析１： 名称 Enzyme A *(nt 697 - 1000);
解析塩基数 ３０４ｂｐ
解析２： 名称 Enzyme A" *(nt 479 - 780)
解析塩基数 ３０２ｂｐ

(PCR Primer を含めて PCR 生成物の全体について配列決定願います)

[注 *：Enzyme A 及び Enzyme A"は、米国特許出願番号 09/470,667 の優先権主張の基礎となるヨーロッパ特許出願 EP96115001.8 に記述されているように、ゲッチンゲン（ドイツ）の Deutsche Sammlung von Mikroorganismen に寄託されている菌株 DSM 4025 から、依頼人らが遺伝子を同定し、クローニングし、配列決定した新規なアルコール／アルデヒドデヒドロゲナーゼである。]

7. PCR Primer について

解析 1 の Primer

Forward: A697f: 5′- TACGAAGCCC GTTGGATGAC - 3′ (GC 11/20)

Reverse: A1000r: 5′- TCGGGTTGAT CGACTGCAGA - 3′ (GC 11/20)

解析 2 の Primer

Forward: A"479f: 5′- TATTCGACGT CGATCGCGGT - 3′ (GC 11/20)

Reverse: A"780r: 5′- AACTGCTGAG GTGCCGTAGT - 3′ (GC 11/20)

8. その他

[1] Order letter (依頼状、英文 2 部)をご確認戴き、日付及びサインをされたうえ、依頼人宛て 1 通を返送してください。

[2] お送りしました菌株（strain DSM 4025）を添付の培地にて起こし、育成願います。

[3] 上記菌株から chromosomal DNA を調製し、上記解析 1 及び解析 2 のそれぞれの Primer にて増幅してください。

[4] 上記解析 1 及び解析 2 に記載の通りの各 PCR product の配列決定に加え、実験方法、条件及び結果を詳細に記述した実験報告書（英文、実験責任者の日付とサインにより発効されたもの）の作成をお願いします。なお、後日実験責任者の方に宣誓供述書（Declaration）の作成にご協力戴きたく存じます。

以上

Declaration of Material
Exhibit-4 (4/4) (continued)

Declaration Y. Minato
Exhibit-5 (1/2)

[Translation of ORDER FORM]

Sawady Technology Co., LTD.
ORDER FORM for Analysis of Genetic Base Sequence
(Order)

---

1. **Order Date** August 2000

2. **Order person**

Name: Tatsuo Hoshino, Dr.
Organization: Department of Applied Microbiology,
Nippon Roche Research Center, Nippon Roche K.K.
Address 200 Kajiwara, Kamakura-shi, Kanagawa-ken, 247-8530 Japan
TEL : 0467-47-2226 (Ext. 3116) **FAX** :0467-45-6812
(Contact person: Dr. Masako Shinjoh, **e-mail :** masako.shinjoh@roche.com)

3. **Report is addressed to:** Order person directly

4. **Analysis Methods of Sample:**
PCR product direct sequencing [See attached GENERAL PROTOCOLS]

5. **Option :** [See: the description 8. Others below]

6. **Description on the samples to be analyzed:**

Analysis 1: Name Enzyme A* (nt 697 - 1000);
Number of nucleotides 304 bp
Analysis 2: Name Enzyme A" * (nt 479 - 780)
Number of nucleotides 302 bp
(whole PCR products should be sequenced with the primers for PCR)
[Note *: Enzyme A and Enzyme A" are novel alcohol/aldehyde dehydrogenases which the ordering person et al. identified the genes and cloned and sequenced from the strain of DSM 4025 deposited before Deutsche Sammlung von Mikroorganismen in Göttingen (Germany) as described in the patent application EP 96115001.8 which is a priority application of USSN 09/470,667.]

7. **The sequencing primers for 5**

Primer for Analysis 1

A697f: 5′- TACGAAGCCC GTTGGATGAC - 3′ (GC 11/20)

A1000r: 5′- TCGGGTTGAT CGACTGCAGA - 3′ (GC 11/20)

Primer for Analysis 2

A"479f: 5′- TATTCGACGT CGATCGCGGT - 3′ (GC 11/20)

A"780r: 5′- AACTGCTGAG GTGCCGTAGT - 3′ (GC 11/20)

8. **Others**

[1] Please confirm the contents of our Order letter (two copies in English), and after dating and signature please send one copy back to us.

[2] Please cultivate the strain DSM 4025, which we sent, on the cultivation medium attached.

[3] Please prepare the chromosomal DNA from the above strain and amplify the DNAs by using the primers identified in the above Analysis 1 and Analysis 2, respectively and

[4] Please prepare an experimental report (in Japanese) describing the experimental method, conditions and results in detail, which report should be executed by the person responsible to the experiment, as well as the sequencing of the respective PCR products as described in the above Analysis 1 and Analysis 2. Incidentally, we would kindly ask you to cooperate us in preparing a Declaration of your responsible person in this experiment later.

End

Declaration Y. Murata
Exhibit-5 (2/2)

Declaration of ... Exhibit-6

GENERAL PROTOCOLS

Roche's request to Sawady Technology Co. Ltd.

The flow of the actions that Nippon Roche Research Center (Roche) and Sawady Technology Co. LTD. (SAWADY) will take are as described below:

- Roche will send SAWADY the following two materials:

  (1) one ampule of the strain DSM 4025 newly furnished from DSMZ; and

  (2) two agar plates (NS2) to recover the strain DSM 4025;

  with three kinds of documents:

  (1) Order letter which includes description of the mutual understanding between Roche and SAWADY;

  (2) The ORDER FORM; and

  (3) The GENERAL PROTOCOLS (this paper) together with its translation.

- SAWADY will be involved in the following actions for the sequencing experiment which is ordered by Roche this time:

  a. Copying the receipt of the strain DSM 4025 and papers attached thereto;

  b. Cultivating the strain DSM 4025 preserved in an ampule on the agar plate (NS2) at 27°C for 3-5 days;

  c. Preparing the chromosomal DNA from the culture obtained through the above b;

  d. Synthesizing two pairs of the primers (A697f , A1000r , A"479f and A"780r) identified in the ORDER FORM;

  e. Amplifying the target two regions by PCR with the respective pairs of the primers;

  f. Performing direct sequencing of the PCR products, respectively;

  g. Preparing an experiment report (which describes the precise protocols used to sequence the PCR products and the results); and

  h. Sending (a) and (g) mentioned above to Roche.

End

Declaration Kimata

Exhibit-7

[訳文]

ジェネラル プロトコール
サワデーテクノロジーに対するロシュの依頼事項

日本ロシュ研究所（Roche）及び株式会社サワディー・テクノロジー（SAWADY）が執り行う手続きの流れは、次の通りです。

- Roche は、次の２種類の材料：

（１）DSMZ から新たに分譲を受けた菌株 DSM 4025 のアンプル１本、及び

（２）菌株 DSM 4025 を起こすための２個の寒天平板培地(NS2)；を

次の３種類の文書；

（１）Roche 及び SAWADY の間の相互理解事項の記載を含む依頼状；

（２）依頼書；及び

（３）訳文が添付されたジェネラル プロトコール（この書面）

と共に SAWADY に送付します。

- SAWADY は今回 Roche が依頼する配列決定実験に際して次の手続きを含めてお執り進め願います：

ａ．菌株 DSM 4025 の受領書及び菌株に添付された書面の写し作成；

ｂ．アンプル中に保存された菌株 DSM 4025 を、寒天平板培地(NS2)上にて、２５℃で、３～５日間培養；

ｃ．上記ｂにて得られた培養物からの染色体ＤＮＡの調製；

ｄ．ORDER FORM に特定しました２対のプライマー(A697f , A1000r , A"479f 及び A"780r)の合成；

ｅ．それぞれのプライマー対を用いて PCR により２つの標的領域を増幅；

ｆ．それぞれの PCR 生成物の直接配列決定の実施；

ｇ．実験報告書（PCR 生成物の配列決定に使用した正確なプロトコール、及び結果を記述する）の作成；並びに

ｈ．上記(a)及び(g) の書類の Roche への送付。

以上

received
Aug. 27, 2002
M. Shinjoh

Sawady → → → KOLA
KOLA御中

注文書

サワディー管理番号 SW-002

お客様名 新城 様 平成 12年 8月 17 日
所属 日本ロシュ研究所
住所 神奈川県鎌倉市梶原200
Tel Fax
Email

依頼内容: ・菌体よりクロモゾームDNA抽出

納品状態:

サンプル: 菌体
DSM4025 (凍結乾燥品)
N2寒天培地 (2枚)
取り扱い説明書

Declaration K. Murata
Exhibit -8

備考:

その他、連絡事項

KOLA記入欄

予定納期 その他サワディーへの連絡事項等

内容をご確認いただき、ご不明の点はご連絡をいただけますようにお願いいたします。

(株)サワディーテクノロジー
〒171-0022 東京都豊島区南池袋2-9-9 第一池袋ホワイトビル1F
Tel: 03-3988-4633 Fax: 03-3982-5666
Email: product@sawady.com 担当／中川 温子

[T5] Order letter from Sawady to Kyurin dated Aug. 17, 2000

Four pages including this page.
Sawady to KOLA

To KOLA

ORDER SHEET

Sawady No. SW-002
Aug. 17, 2000

Client name: Dr. Shinjoh
Organization: Nippon Roche Research Center
Address: 200 Kajiwara Kamakura Kanagawa

Order: Extraction of chromosomal DNA from cells
Shipping form:
Sample: Cells
DSM4025 (Lyophilized)
N2** agar plates
Protocols
Others: Other information
KOLA memo: Planned delivery date Other information to Sawady

Please confirm the items and let us know if you have any questions.

K.K. Sawady Technology
171-0022 Dai-ichi Ikebukuro White Building 1F
2-9-9, Minami-Ikebukuro, Toshima-ku, Tokyo
Tel; 03-3988-4633 Fax; 03-3982-5666
Email:product@sawady.com Atsuko Nakagawa

Declaration Y. Murata
Exhibit-9

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67/90